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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/046,433	Applicant(s) NI ET AL.	
	Examiner Eileen O'Hara	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7,10,13,16,19-21,23,28-30,33-38,40,44,46 and 64-131* is/are pending in the application.

4a) Of the above claim(s) *33,40,44 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 7, 10, 13, 16, 19-21, 23, 28-30, 34-38 and 64-131* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *See Continuation Sheet* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continuation of Disposition of Claims: Claims subject to restriction and/or election requirement are 1,4,7,10,13,16,19-21,23,28-30,33-38,40,44,46 and 64-131.

DETAILED ACTION

1. Claims 1, 4, 7, 10, 13, 16, 19-21, 23, 28-30, 33-38, 40, 44, 46 and 64-131 are pending in the instant application. Claims 1, 7 and 33 have been amended, claims 2, 3, 5, 6, 8, 9, 11, 12, 14, 15, 17, 18, 22, 24-27, 31, 32, 39, 41-43, 45 and 47-63 have been canceled and claims 64-131 have been added as requested by Applicant in Paper Number 7, filed February 10, 2003.

Election/Restriction

2. Applicant's election with traverse of Group A in Paper No. 7 is acknowledged. The traversal on pages 13-14 of the response is on the ground(s) that MPEP § 803 lists the criteria for a proper restriction as an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate patents and they are either independent or distinct, and if the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions. It is acknowledged that the claims of Group G were mistakenly included in the restriction. Applicants also assert that as Groups D, E and F are in the same class and subclass, this indicates that they have not acquired a separate status in the art, and therefore they would not present a serious burden to search and examine together. Applicants also assert that to search Groups I-VII would not be a serious burden on the examiner, and that since the different groups are directed to portions of the same sequences (SEQ ID NOS: 1, 4, 39 and 60), a search of each of the groups would largely, if not entirely, overlap, and that a search for sequence of group A, polypeptides of group B, antibodies of group C and methods of treatment of groups D, E and F would overlap, the search and examination of all these groups would not entail a serious burden.

This is not found persuasive because consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search:. These criteria were met for groups A-C in the above restriction. A search for antibodies to a protein would constitute a different search than that of a search for the protein. It is old and well known in the art that antibodies have been generated without having purified protein, and antibodies to one protein may also cross-react with a related protein. Although groups D-F are classified together as methods of treatment, they are methods of treatments with different compounds, having different structures, activities and effects, and would require separate consideration. As stated in the MPEP § 803, "a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02.". Further, a search is directed not only to art which would be anticipatory, but also to art that would render the invention obvious. Additionally, the sequences of SEQ ID NOS: 1, 4, 39 and 60 are not portions of the same sequences: SEQ ID NOS: 1 and 39 are sequences encoding a TR13 protein, while SEQ ID NOS: 4 and 60 are sequences encoding a TR14 protein, which are completely different proteins, and so are not portions of the same sequences. Thus, the groups require divergent searches, and to search all inventions would be burdensome.

Applicant's election with traverse within Group A of a TR13 nucleic acid of SEQ ID NO: 39 encoding a polypeptide of SEQ ID NO: 40 is acknowledged. The traversal on pages 15-16 of the response is on the ground(s) that the Examiner has not disclosed any statutory or regulatory basis for the further restriction within the provisionally elected group A. Applicants note that the Examiner is requiring an election of group members of the Markush-type claims, and point out that MPEP § 803.02 requires that if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all claims on the merits. Applicants submit that the members of the Markush groups of the pending claims to provisionally elected group A are sufficiently few in number and very closely related, as they are all different portions of the same polynucleotide sequences, so that a search of all of the members may be made without a serious burden, and point out that MPEP § 803.04 holds that even when nucleotide sequence encoding different proteins are contained in an application, a reasonable number, normally ten sequences, will be examined in a single application. Applicants submit that the instant nucleic acids encode different fragments of the same proteins rather than different proteins as contemplated by § 803.04, and that section 803.04 further states that "nucleotide sequences encoding the same protein are not considered to be independent and distinct inventions and will continue to be examined together." Applicants further submit that a reasonable number of such nucleic acids should be examined together, and the Examiner has given no indication why ten sequences are unreasonable in the present case.

Applicants' arguments have been fully considered but are not deemed persuasive. As discussed above, the sequences of SEQ ID NOS: 1, 4, 39 and 60 are not portions of the same

sequences: SEQ ID NOS: 1 and 39 are sequences encoding a TR13 protein, while SEQ ID NOS: 4 and 60 are sequences encoding a TR14 protein, which are completely different proteins, and so are not portions of the same sequences. Additionally, the nucleic acid sequences of SEQ ID NOS: 8-17 and 48-59 are also distinct and independent from each other in that the nucleic acid molecules of each group of inventions have unique nucleotide sequences that are different and require separate and non-coextensive searches. Applicant on page 26 of the specification states that the nucleic acids of SEQ ID NOS: 8-17 and 48-59 are related to portions of the nucleotide sequences of SEQ ID NO: 1 and 39 respectively, however, it is not clearly defined how they are related, and they appear to be different and require separate sequence searches and consideration.

It is additionally pointed out that the search and examination of each of the groups, which searches and examinations are not-co-extensive, are not required one for the other. Thus, contrary to applicant's position, the search and examination of each group would indeed pose a serious burden for the examination. Also argued is that a search for one group would be overlapping and provide useful information about the other groups. However, the fact that some useful information may be obtained in the searches of one group for that of another group, and the fact that there may possibly be overlaps in the searches is not a sufficient basis for holding the restriction to be improper, because the search and examination of one group may not yield all of the necessary information for the other group. As to Applicants' arguments that a reasonable number of sequences, up to ten, should be examined together, the U.S.P.T.O considers a search for more than one nucleic acid sequence a burden because the Office would have to search several different databases for the separate sequences, which would be a serious burden on the examiner and the office, especially considering the enormous numbers of sequences currently

deposited in the sequence databases, which is continuing to grow at a logarithmic rate. Additionally, although the proteins of SEQ ID NOS: 2 and 40 may be related, they are splice variants, and are encoded by portions of the same DNA, but would still require separate search and consideration. For example, although the protein of SEQ ID NO: 2 is the same from amino acids 47-705 to amino acids 298-1001 of the protein of SEQ ID NO: 40, SEQ ID NO: 2 is different at both the amino terminal and carboxy terminal ends of the protein from that of the protein of SEQ ID NO: 40 (30% different in the extracellular domain). Therefore, the proteins are different as are the encoding nucleic acids. Thus, to search all inventions would be burdensome.

The requirement is still deemed proper and is therefore made FINAL.

Claims 33, 40, 44 and 46 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claims 1, 4, 7, 10, 13, 16, 19-21, 23, 28-30, 34-38 and 64-131 are currently under examination and will be examined in so far as they encompass nucleic acid encoding polypeptide of SEQ ID NO: 40.

Priority Statement in Specification

3. The filing date of provisional application 60/149,450 is incorrectly written as July 18, 1999 in the first paragraph of the specification. The actual filing date is August 18, 1999. Appropriate correction is required.

Information Disclosure Statement

4.1 Applicants are advised that reference AB in the IDS filed Dec. 11, 2001 appears to be the incorrect reference, since there is no inventor named Rosen and there are no sequences in the published application 20030058697.

4.2 The sequences disclosed in the IDS (references BA, BC-EB) have been considered to the extent that was possible absent an explanation of relevance or a sequence alignment.

Specification

5. The disclosure is objected to because of the following informalities:

5.1 Under the Brief Description of the Figures starting at page 10, the number of pages referred to for some of the figures are incorrect. Figures 1A-C should be changed to Figures 1A-D, Figures 2A-C should be changed to 2A-D, Figures 4A-D should be changed to Figures 4A-E, Figures 7A-D should be changed to Figures 7A-E, and Figures 8A-B should be changed to Figures 8A-D to correspond to the Figure. These corrections should also be made elsewhere in the specification where the figures are recited, for example on page 5.

5.2 On page 94, line 14, the transmembrane domain of SEQ ID NO: 40 is identified as amino acids 134-150, but elsewhere in the specfication the transmembrane domain is identified as amino acids 907-931 of SEQ ID NO: 40.

5.3 On page 94, lines 17-19, the extracellular domain of SEQ ID NO: 40 is identified as amino acids 42-96, but elsewhere in the specification is identified as amino acids 42-906.

Appropriate correction is required.

5.4 The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Nucleic Acids encoding TR13 Receptor.

Claim Objections

6. Claims 1, 20, 21 and 23 are objected to because of the following informalities: they encompass non-elected inventions which should be deleted. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7.1 Claims 1, 13, 16, 19 and 104-131 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants' referral to the deposit of PTA-507 (HWLHN83) on page 5 of the specification is an insufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met. If the deposits were made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all

restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State.

7.2 Claims 1, 20, 21, 23, 28-30, 34-38, 64, 65, 68, 71, 74-77, 80, 83, 86-105, 107, 109, 111, 113, 115 and 117-130 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification describes a polypeptide sequence consisting of SEQ ID NO: 40, which is shown to have the following activity: binding Fas ligand. However, the claims as written include polypeptides comprising fragments and homologues, encompass polypeptides that vary substantially in length and also in amino acid composition. The instant disclosure of a polypeptide, that of SEQ ID NO: 40, and a variant of that polypeptide, SEQ ID NO: 2, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the

written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Receptor function cannot be reliably predicted from protein sequence homology. For example, Transforming Growth Factor (TGF-beta) Family OP-1 induces metanephrongenesis whereas closely related TGF-beta family members-BMP-2 and TGF-beta1-have no effect on metanephrogenesis under identical conditions (Vukicevic et al., 1996, PNAS USA 93:9021-9026). Platelet-derived Growth Factor (PDGF) Family VEGF, a member of the PDGF family, is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells while PDGF is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (Tischer et al., U.S. Patent 5,194,596, column 2, line 46 to column 3, line 2). Finally, vertebrate growth hormone of 198 amino acids becomes an antagonist (inhibitor of growth) when a single amino acid is changed (Kopchick et al, U.S. Patent No. 5,350,836).

Even 99% homology does allow predictability in this instance. Given the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences. Since the critical feature of the protein is the extracellular domain, which binds FAS ligand, nucleic acid molecules comprising a polynucleotide encoding the extracellular domain have adequate written description; however, nucleic acid molecules that do not encode the extracellular domain, or encode a polypeptide 95% identical to the extracellular domain or truncated versions of it (for example, claims 103 (d) and (h) and claims 74-76 and 86-88 in which the polynucleotide encodes a polypeptide missing approximately one third of the amino terminus of the extracellular domain) do not have adequate written description, since this region is more likely than not to be critical for Fas ligand binding. The claims encompass a broader genus than the Applicants have defined. The instantly claimed genus is not so limited and the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polynucleotides encompassed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 4, 7, 10, 13, 16, 19-21, 23, 28, 30 and 34-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4, 7, 10, 13, 16, 19-21, 23, 28, 30 and 34-38 are indefinite because claim 1 recites a nucleotide sequence encoding **the** TR13 extracellular or intracellular domain, and there are two TR13 proteins disclosed that have different extracellular and intracellular domains, so it is not clear which TR13 extracellular and intracellular domains are being claimed.

Priority

35 U.S.C. § 120 states that:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

35 U.S.C. § 119(e) states that:

> An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

9. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 or § 119(e) from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, which respect to the now claimed invention. Applicants for the first time have supplied a specific and substantial utility, that of binding Fas Ligand, which was not contemplated or disclosed in the parent applications. Because the parent application, 09/618,570 does not meet the requirements of 35 U.S.C. § 112, first paragraph, for those reasons given in the Office Actions, Paper Nos. 10, 14 and 17, the prior application and the prior provisional

applications do not meet those requirements and, therefore, are unavailable under 35 U.S.C. § 120 or § 119(e). The effective priority date of the instant application is considered to be the filing date of this application, Jan. 16, 2002, because the parent applications were not supported by either a specific and substantial utility or a well established utility.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10.1 Claims 1, 4, 7, 10, 13, 16, 19-21, 23, 29-30, 34-38, 64, 65, 68, 71, 74, 75, 77, 80, 83, 86-96, 98-105, 107, 109, 111, 113, 115, 117-124, 126-130 are rejected under 35 U.S.C. 102(b) as being anticipated by Bruck et al., WO 00/58460, October 5, 2000.

Claims 1, 4, 7, 10, 13, 16, 19-21, 23, 29-30, 34-38, 64, 65, 68, 71, 74, 75, 77, 80, 83, 86-96, 98-105, 107, 109, 111, 113, 115, 117-124, 126-130 encompass nucleic acid molecules comprising a polynucleotide having a nucleotide sequence at least 95% identical to a nucleotide sequence encoding the full-length or recited portions (including epitope-bearing portion) of the polypeptide of SEQ ID NO: 40 or the nucleotide sequence of SEQ ID NO: 39 (cDNA clone contained in ATCC Deposit No. PTA-507), complements thereof, or nucleic acids molecules that hybridize under stringent hybridization conditions (defined in the specification on page 88, section 0120), wherein the nucleic acid can be DNA, RNA, double-stranded, single-stranded,

compositions comprising nucleic acid molecules and a carrier, nucleic acid molecules encoding fusion proteins which may comprise human IgG Fc region, expression vectors, host cells and method of recombinantly producing protein.

Bruck et al. disclose a nucleic acid molecule (SEQ ID NO: 1) that is 97.8% identical to the nucleic acid sequence of SEQ ID NO: 39 of the instant application, and encodes a protein (SEQ ID NO: 2) that is 97.6% identical to amino acids 1-1001 and 100% identical to amino acids 169-978 of SEQ ID NO: 40 of the instant application (see attached sequence alignments). Bruck et al. also teach nucleic acids encoding epitopes (page 2, lines 12-29), fusion proteins comprising IgG Fc region (page 5, lines 21-29, page 6, lines 14-32), recombinant production of polypeptide, expression vectors and host cells genetically engineered to produce protein (page 8, lines 1-5, page 13, line 20 page 14, line 30, page 14, line 12 to page 15, line 22), composition comprising nucleic acid and a carrier (page 16, lines 4-18), vectors, complementary polynucleotides (page 8, line 32 to page 9, line 4), mRNA, double-stranded (cDNA and genomic clones), single stranded (primers) (page 11, lines 24-27 to page 12, line 28, page 21, lines 16-25, page 27, lines 31-33). Also see claims 8-16 and 18. Although Bruck et al. do not specifically state that the nucleic acid molecule is operably associated with a heterologous regulatory sequence that controls gene expression, one of ordinary skill in the art knows that expression vectors, by definition, have regulatory sequences that allow gene expression. Therefore, Bruck et al. anticipates the claims.

10.2 Claims 21 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Edwards et al., US Patent No. 5,736,363, April 7, 1998.

Claims 21 and 23 encompass an isolated nucleic acid molecule comprising a polynucleotide which encodes the amino acid sequence of an epitope-bearing portion of a TR13

receptor of claim 1 or epitope-bearing portion of amino acids 437-789 of SEQ ID NO: 40. The specification on page 173, section 0266, states: "Antigenic epitope-bearing peptides and polypeptides of the invention preferably contain a sequence of at least seven,.....amino acids contained within the amino acid sequence of a polypeptide of the invention."

Edwards et al. disclose a nucleic acid molecule (SEQ ID NO: 9) that encodes a polypeptide (SEQ ID NO: 10) comprising an amino acid sequence (amino acids 110-117 of SEQ ID NO: 10) that is identical to amino acids 680-687 of SEQ ID NO: 40 of the instant application. Since an epitope-bearing peptide can comprise at least 7 amino acids, the nucleic acid molecule encoding the polypeptide comprising the 8 amino acid portion of Edwards meets the limitations of the claims.

10.3 Claims 1, 4, 7, 10, 13, 16, 19-21, 23, 28-30, 34-38 and 64-131 are rejected under 35 U.S.C. 102(a) as being anticipated by Ruben et al., WO 01/05834, January 25, 2001.

Claims 1, 4, 7, 10, 13, 16, 19-21, 23, 28-30, 34-38 and 64-131 encompass nucleic acid molecules comprising a polynucleotide having a nucleotide sequence encoding the full-length or recited portions (including epitope-bearing portion) of the polypeptide of SEQ ID NO: 40 or the nucleotide sequence of SEQ ID NO: 39 (cDNA clone contained in ATCC Deposit No. PTA-507), complements thereof, wherein the nucleic acid can be DNA, RNA, double-stranded, single-stranded, compositions comprising nucleic acid molecules and a carrier, nucleic acid molecules encoding fusion proteins which may comprise human IgG Fc region or human serum albumin, expression vectors, host cells and method of recombinantly producing protein.

Ruben et al. discloses a nucleic molecule comprising a polynucleotide having a nucleotide sequence encoding the polypeptide of SEQ ID NO: 40 and the nucleotide sequence of

SEQ ID NO: 39 (cDNA clone contained in ATCC Deposit No. PTA-507), complements thereof, wherein the nucleic acid can be DNA, RNA, double-stranded, single-stranded, compositions comprising nucleic acid molecules and a carrier, nucleic acid molecules encoding fusion proteins which may comprise human IgG Fc region or human serum albumin, expression vectors, host cells and method of recombinantly producing protein. Although this reference is Applicants' own published PCT and claims priority back to some of the same provisional applications as the instant application, because the instant application is only accorded an effective priority date of January 16, 2002, the reference is considered prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 97 and 125 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bruck et al., WO 00/58460, October 5, 2000, in view of Fleer et al., PN 5,876,969.

Claims 97 and 125 encompass nucleic acid molecules of the instant invention encoding a fusion protein comprising human serum albumin as the heterologous polypeptide. The teachings of Bruck et al. are summarized as above. Bruck et al. does not disclose a nucleic acids encoding a fusion protein comprising human serum albumin.

Fleer et al. disclose that it is useful to make fusion proteins comprising biologically active polypeptides fused to human serum albumin, because the human serum albumin has a high plasma half-life and makes it possible to maintain in the body, a given biological activity for prolonged period, and make it possible to reduce administered doses and therefore side effects following a higher administration (see entire patent, especially column 1, lines 14 to column 2, line 10).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use the nucleic acid molecules of Bruck et al. to make a fusion polypeptide with human serum albumin, as taught by Fleer et al., in view of Fleer et al.'s suggestion that it would be desirable to do so, for the reasons cited above. The skilled artisan would be motivated to do so in order to produce a polypeptide that remains biologically active and that could possibly have improved pharmacological properties. There would be a reasonable expectation of success, since fusion proteins have been widely and successfully used in the field of molecular biology, and because Fleer et al. demonstrates that a fusion protein comprising human serum albumin favorably modifies the pharmacokinetic properties of the polypeptide fused to human serum albumin.

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Patent Examiner

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